

CLAIMS

1. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D-E, wherein

A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes an immunoglobulin constant region-like domain,

D comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a transmembrane domain, and

E comprises a nucleotide sequence of at least one fifth exon of a T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a cytoplasmic domain,

with the proviso that E does not comprise a nucleotide sequence selected from a group consisting of SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29 and SEQ ID NO:31.

2. The isolated nucleic acid of claim 1 which is a cDNA.

3. The isolated nucleic acid of claim 2 which comprises a coding region of the cDNA.

4. The isolated nucleic acid of claim 1, wherein the nucleotide sequence is derived from a T cell costimulatory molecule gene encoding B7-1.

5. The isolated nucleic acid of claim 4, wherein B7-1 is murine.

6. The isolated nucleic acid of claim 4, wherein B7-1 is human.

7. The isolated nucleic acid of claim 5, wherein E comprises a nucleotide sequence shown in SEQ ID NO:4.

8. The isolated nucleic acid of claim 5, wherein E comprises a nucleotide sequence encoding an amino acid sequence shown in SEQ ID NO:5.

5 9. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 and is encoded by a T cell costimulatory molecule gene having

at least one first exon encoding a first cytoplasmic domain comprising a nucleotide sequence selected from the group consisting of a nucleotide sequence of SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29 and SEQ ID NO:31, and

10 at least one second exon encoding a second cytoplasmic domain, wherein the isolated nucleic acid comprises a nucleotide sequence encoding the second cytoplasmic domain.

15 10. The isolated nucleic acid of claim 9 which comprises a coding region of a cDNA.

11. The isolated nucleic acid of claim 9 which does not comprise a nucleotide sequence encoding the first cytoplasmic domain.

20 12. The isolated nucleic acid of claim 9 wherein the T cell costimulatory molecule gene is B7-1.

13. The isolated nucleic acid of claim 12 wherein B7-1 is murine.

25 14. The isolated nucleic acid of claim 12 wherein B7-1 is human.

15. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:1.

30 16. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:3.

35 17. An isolated nucleic acid encoding a cytoplasmic domain derived from a protein which binds CD28 or CTLA4, the nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:4.

960E80 52520/80

18. An isolated protein which binds to CD28 or CTLA4 having an amino acid sequence derived from amino acid sequences encoded by at least one T cell costimulatory molecule gene, the protein comprising a contiguous amino acid sequence represented by a formula A-B-C-D-E, wherein

A, which may or may not be present, comprises an amino acid sequence of a signal peptide domain encoded by at least one exon of a T cell costimulatory molecule gene,

B comprises an amino acid sequence of an immunoglobulin variable region-like domain encoded by at least one exon of a T cell costimulatory molecule gene,

C comprises an amino acid sequence of an immunoglobulin constant region-like domain encoded by at least one exon of a T cell costimulatory molecule gene,

D comprises an amino acid sequence of a transmembrane domain encoded by at least one exon of a T cell costimulatory molecule gene, and

E comprises an amino acid sequence of a cytoplasmic domain encoded by at least one exon of a T cell costimulatory molecule gene,

with the proviso that E not comprise an amino acid sequence selected from the group consisting of SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30 and SEQ ID NO:32.

19. The isolated protein of claim 18 which is B7-1.

20. The isolated protein of claim 19 which is murine.

21. The isolated protein of claim 19 which is human.

22. The isolated protein of claim 20, wherein E comprises an amino acid sequence shown in SEQ ID NO:5.

23. An isolated protein which binds CD28 or CTLA4 and is encoded by a T cell costimulatory molecule gene having
at least one first exon encoding a first cytoplasmic domain comprising an amino acid sequence selected from the group consisting of an amino acid sequence of SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, and SEQ ID NO:32, and

at least one second exon encoding a second cytoplasmic domain,
wherein the T cell costimulatory molecule comprises the second cytoplasmic domain.

24. The isolated protein of claim 23 which does not comprise the first cytoplasmic domain.

25. The isolated protein of claim 23 which is B7-1.

26. The isolated protein of claim 25 which is murine.

27. The isolated protein of claim 25 which is human.

28. An isolated protein which binds CD28 or CTLA4 comprising an amino acid sequence shown in SEQ ID NO:2.

29. An isolated cytoplasmic domain polypeptide derived from a protein which binds CD28 or CTLA4, the polypeptide comprising an amino acid sequence shown in SEQ ID NO:5.

30. A recombinant expression vector comprising the nucleic acid molecule of claim 15.

31. A host cell which contains the recombinant expression vector of claim 30.

32. An antibody which binds to the murine B7-1 cytoplasmic domain polypeptide of claim 29.

33. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D-E, wherein

A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes an immunoglobulin constant region-like domain,

D, which may or may not be present, comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a transmembrane domain, and

08702525.083095
960220

Sub
a2

E, which may or may not be present, comprises a nucleotide sequence of at least one fifth exon of a T cell costimulatory molecule gene, wherein the at least one fifth exon encodes a cytoplasmic domain,

with the proviso that A does not comprise a nucleotide sequence selected from a group consisting of SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39 and SEQ ID NO:41.

34. The isolated nucleic acid of claim 33 which is a cDNA.

35. The isolated nucleic acid of claim 34 which comprises a coding region of the cDNA.

36. The isolated nucleic acid of claim 33, wherein the nucleotide sequence is derived from a T cell costimulatory molecule gene encoding B7-2.

37. The isolated nucleic acid of claim 36, wherein B7-2 is murine.

38. The isolated nucleic acid of claim 36, wherein B7-2 is human.

39. The isolated nucleic acid of claim 37, wherein A comprises a nucleotide sequence shown in SEQ ID NO:14.

40. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 and is encoded by a T cell costimulatory molecule gene having

at least one first exon encoding a first signal peptide domain comprising a nucleotide sequence selected from the group consisting of a nucleotide sequence of SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39 and SEQ ID NO:41, and

at least one second exon encoding a second signal peptide domain,

wherein the isolated nucleic acid comprises a nucleotide sequence encoding the second signal peptide domain.

41. The isolated nucleic acid of claim 40 which comprises a coding region of a cDNA.

42. The isolated nucleic acid of claim 40 which does not comprise a nucleotide sequence encoding the first signal peptide domain.

Sub
a3⁵
Sub
a4

08702525-083096
960230-5220280

Sub
a4

43. The isolated nucleic acid of claim 40 wherein the T cell costimulatory molecule gene is B7-2.

44. The isolated nucleic acid of claim 43 wherein B7-2 is murine.

45. The isolated nucleic acid of claim 43 wherein B7-2 is human.

46. An isolated nucleic acid encoding a protein which binds CD28 or CTLA4 comprising a nucleotide sequence shown in SEQ ID NO:12.

47. An isolated nucleic acid encoding a signal peptide domain derived from a protein which binds CD28 or CTLA4, the nucleic acid comprising a nucleotide sequence shown in SEQ ID NO:14.

48. An isolated protein which binds CD28 or CTLA4 having an amino acid sequence derived from amino acid sequences encoded by at least one T cell costimulatory molecule gene, the protein comprising a contiguous amino acid sequence represented by a formula A-B-C-D-E, wherein

A comprises an amino acid sequence of a signal peptide domain encoded by at least one exon of a T cell costimulatory molecule gene,

B comprises an amino acid sequence of an immunoglobulin variable region-like domain encoded by at least one exon of a T cell costimulatory molecule gene,

C comprises an amino acid sequence of an immunoglobulin constant region-like domain encoded by at least one exon of a T cell costimulatory molecule gene,

D, which may or may not be present, comprises an amino acid sequence of a transmembrane domain encoded by at least one exon of a T cell costimulatory molecule gene, and

E, which may or may not be present, comprises an amino acid sequence of a cytoplasmic domain encoded by at least one exon of a T cell costimulatory molecule gene,

with the proviso that A not comprise an amino acid sequence selected from the group consisting of SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40 and SEQ ID NO: 42.

49. The isolated protein of claim 48 which is B7-2.

50. The isolated protein of claim 49 which is murine.

51. The isolated protein of claim 49 which is human.

52. The isolated protein of claim 50, wherein A comprises an amino acid sequence
5 shown in SEQ ID NO: 15.

53. An isolated protein which binds CD28 or CTLA4 and is encoded by a T cell
costimulatory molecule gene having

10 at least one first exon encoding a first signal peptide domain comprising an amino
acid sequence selected from the group consisting of an amino acid sequence of SEQ ID
NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40 and SEQ ID NO:42, and
at least one second exon encoding a second signal peptide domain,
wherein the T cell costimulatory molecule comprises the second signal peptide domain.

15 54. The isolated protein of claim 53 which does not comprise the first signal
peptide domain.

55. The isolated protein of claim 53 which is B7-2.

20 56. The isolated protein of claim 55 which is murine.

57. The isolated protein of claim 55 which is human.

25 58. An isolated protein which binds CD28 or CTLA4 comprising an amino acid
sequence shown in SEQ ID NO:13.

59. An isolated signal peptide domain polypeptide derived from a protein which
binds CD28 or CTLA4, the polypeptide comprising an amino acid sequence shown in SEQ
ID NO:15.

30 60. A recombinant expression vector comprising the nucleic acid molecule of
claim 46.

35 61. A host cell which contains the recombinant expression vector of claim 60.

62. An antibody which binds to the polypeptide of claim 59.

03702525-033096

63. An isolated nucleic acid encoding a protein comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D, wherein

5 A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

10 B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin constant region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes a transmembrane domain, and

15 D comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a cytoplasmic domain.

20 64. The isolated nucleic acid of claim 63 comprising a nucleotide sequence shown in SEQ ID NO:8.

25 65. The isolated nucleic acid of claim 63 comprising a nucleotide sequence shown in SEQ ID NO:10.

30 66. An isolated protein having an amino acid sequence derived from amino acid sequences encoded by at least one T cell costimulatory molecule gene, the protein comprising a contiguous amino acid sequence represented by a formula A-B-C-D, wherein

A, which may or may not be present, comprises an amino acid sequence of a signal peptide domain encoded by at least one exon of a T cell costimulatory molecule gene,

35 B comprises an amino acid sequence of an immunoglobulin constant region-like domain encoded by at least one exon of a T cell costimulatory molecule gene, and

C comprises an amino acid sequence of a transmembrane domain encoded by at least one exon of a T cell costimulatory molecule gene, and

D comprises an amino acid sequence of a cytoplasmic domain encoded by at least one exon of a T cell costimulatory molecule gene.

67. The isolated protein of claim 66 comprising an amino acid sequence shown in SEQ ID NO:9.

68. The isolated protein of claim 66 comprising an amino acid sequence shown in SEQ ID NO:11.

5 ~~69. An isolated nucleic acid encoding a protein comprising a contiguous nucleotide sequence derived from at least one T cell costimulatory molecule gene, the nucleotide sequence represented by a formula A-B-C-D, wherein~~

10 A comprises a nucleotide sequence of at least one first exon of a T cell costimulatory molecule gene, wherein the at least one first exon encodes a signal peptide domain,

15 B comprises a nucleotide sequence of at least one second exon of a T cell costimulatory molecule gene, wherein the at least one second exon encodes an immunoglobulin variable region-like domain,

C comprises a nucleotide sequence of at least one third exon of a T cell costimulatory molecule gene, wherein the at least one third exon encodes a transmembrane domain, and

20 D comprises a nucleotide sequence of at least one fourth exon of a T cell costimulatory molecule gene, wherein the at least one fourth exon encodes a cytoplasmic domain.

70. The isolated nucleic acid of claim 69 comprising a nucleotide sequence shown in SEQ ID NO:62.

25 ~~71. The isolated nucleic acid of claim 69 comprising a nucleotide sequence shown in SEQ ID NO:64.~~

30 72. An isolated protein having an amino acid sequence derived from amino acid sequences encoded by at least one T cell costimulatory molecule gene, the protein comprising a contiguous amino acid sequence represented by a formula A-B-C-D, wherein

35 A, which may or may not be present, comprises an amino acid sequence of a signal peptide domain encoded by at least one exon of a T cell costimulatory molecule gene,

B comprises an amino acid sequence of an immunoglobulin variable region-like domain encoded by at least one exon of a T cell costimulatory molecule gene, and

C comprises an amino acid sequence of a transmembrane domain encoded by at least one exon of a T cell costimulatory molecule gene, and

D comprises an amino acid sequence of a cytoplasmic domain encoded by at least one exon of a T cell costimulatory molecule gene.

73. The isolated protein of claim 72 comprising an amino acid sequence shown in
5 SEQ ID NO:63.

74. The isolated protein of claim 72 comprising an amino acid sequence shown in
SEQ ID NO:65.

10 75. A recombinant expression vector comprising the nucleic acid molecule of
claim 69.

76. A host cell which contains the recombinant expression vector of claim 75.

add
as

add
as

08702525 08300
960E80 52520280